April 1998

Department of Health Services
S. Kimberly Belshé, Director

California Morbidity

State of California
Pete Wilson, Governor

Health Effects of Toxin-Producing Indoor Molds in California

Due to excessive rainfall this winter, many Californians are experiencing increased exposure to indoor microorganisms. Several fungal species capable of producing toxic substances have been found in water-damaged California homes and offices. This article provides information about potential health effects from exposure to *Stachybotrys chartarum* (a.k.a. *S. atra*), a toxigenic mold that has received increasing attention recently among indoor air researchers and the public. Within the last 12-18 months, several scientific reports (and media attention) have focused on *Stachybotrys*, a ubiquitous saprophytic fungus that grows on nitrogen-poor, cellulose-rich materials such as hay, straw and building materials (ceiling tiles, wallpaper, paper covering on gypsum wallboard). The statewide prevalence of this fungus in homes or workplaces is unknown, although one report found Stachybotrys in 2-3% of a small survey of southern California homes.[1]

Mechanism of Action

Some strains of *Stachybotrys chartarum* can produce mycotoxins of the trichothecene and spirolactone families. The trichothecene mycotoxins satratoxins G and H are potent protein synthesis inhibitors and cause immunosuppression in laboratory animals. In experimental animal studies, the trichothecenes affect rapidly proliferating tissues such as skin and mucosa, as well as lymphatic and hematopoietic tissues.[2] In laboratory animals, acute exposure to large amounts of trichothecene toxins results in a rapid release of sequestered white blood cells into circulation, while repeated or chronic exposure destroys granulocytic precursor cells in bone marrow leading to white cell depletion. Among the reported cellular effects are: mitogen B/T lymphocyte blastogenesis suppression; decrease of IgM, IgG, IgA; impaired macrophage activity and migration-chemotaxis; broad immunosuppressive effects on the cellular and humoral-mediated immune response leading to secondary infections; and, paradoxically, increased spontaneous antibody producing cells in the spleen.[3]

Toxigenic strains of *Stachybotrys chartarum* may also produce spirolactones (stachybotrylactone) and spirolactams (stachybotrylactam), toxins which produce anticomplement effects.[4] Possible synergistic effects between the trichothecenes and these mycotoxins have not yet been evaluated. Although laboratories can test a sample of *Stachybotrys chartarum* for its ability to produce mycotoxins, *in vitro* results do not necessarily equate with the *in vivo* situation. Therefore, a fungus that produces toxins in the lab may not do so in the field, or vice versa. It has been suggested that to assure the safety of any exposed individual, whenever *Stachybotrys chartarum* is identified, it should be considered as a potential mycotoxin-producing organism.[5]

Positive skin reactions to the fungus have been found in some asthmatics living or working in *Stachybotrys*-contaminated rooms, suggesting a hypersensitivity component in addition to the potential for mycotoxicosis. Thus the fungal spores themselves or chemicals carried on the spores may produce either allergenic or toxigenic effects.[6]

Routes of Exposure

Due to its wet, slimy growth characteristics, it is unusual for spores from active *Stachybotrys* colonies to become aerosolized. However, when colonies of this fungus die and become dehydrated, there is increased risk for air dispersion. Portals of possible entry into the body include inhalation and dermal absorption when the fungus is found on walls or in carpets.

Case Reports

Historically, toxicologic effects from this fungus were reported in Europe, where horses, sheep and cattle suffered fatal hemorrhagic disorders following ingestion exposures.[7] Human occupational exposures to contaminated straw or hay resulted in nasal and tracheal bleeding, skin irritation and alterations in white blood cell counts.[8]

The first U.S. case of Stachybotrys-associated health effects from inhalation exposure was reported in a suburban Chicago family.[9] The fungus had contaminated the ventilation system and ceilings of the house. Health effects reported by the family included chronic recurring cold and flu-like symptoms, sore throat, diarrhea, headache, fatigue, dermatitis, intermittent focal alopecia and generalized malaise. Workers who cleaned and removed contaminated material from this house also experienced skin irritation and respiratory symptoms. After *Stachybotrys* contamination was removed, the house was reoccupied and residents reported no recurrence of clinical symptoms.

Stachybotrys and satratoxin H (one of the trichothecene mycotoxins) were subsequently identified in a water-damaged office building in New York City. A small case-control study showed workers exposed to the fungus were at statistically significant higher risk for nonspecified disorders of the lower airways, eyes and skin; fevers and flu-like symptoms, and chronic fatigue.[10-11] No significant differences in specific *S. chartarum* IgE and IgG levels were noted between cases and controls. Although *Stachybotrys chartarum* specific IgE (RAST) and IgG (ELISA) tests are available, their sensitivity and specificity have not yet been determined.

A recent report describes identification of 10 likely or possible cases of building-related asthma in a courthouse contaminated with *Stachybotrys* and *Aspergillus* species.[12] Self-reported symptoms among co-workers included fever, headache, rhinitis, coughing, dyspnea and chest tightness. Chest radiographs were negative and *Stachybotrys*-specific serology was uninformative.

Stachybotrys chartarum, along with other fungi and environmental tobacco smoke, was recently postulated to have an association with pulmonary hemosiderosis in a cluster of Cleveland, Ohio infants.[13-14] While *SC* was found more frequently in the homes of case infants compared to controls, exposure of case infants to mycotoxins in the home could not be determined. Because there is no field test for airborne mycotoxins, it is not currently possible to determine if toxins were actually present in the living space of case infants, and if so, at what levels. However, since *Stachybotrys chartarum* spores containing mycotoxins have been shown to produce pulmonary alveolar and intra-bronchiolar inflammation and hemorrhage in mice,[15-16] more research into the inhalation effects of these toxins, especially on immature alveoli and pulmonary vascular walls, is critically needed.

Pulmonary hemosiderosis is a condition characterized by recurrent alveolar hemorrhage resulting in clinical signs of cough, wheeze, hemoptysis, tachypnea, low grade fever, and microcytic hypochromic anemia. Chest radiographs typically show patchy infiltrates and sputum specimens, laryngeal swabs or gastric aspirates reveal hemosiderin-laden macrophages. The association of some cases with allergy to cow's milk (Heiner syndrome) and its association with glomerulonephritis in Goodpasture's syndrome suggest an immunologic etiology but immunologic findings in idiopathic cases have been inconsistent. Some familial case reports also suggest a genetic component.

California Department of Health Services staff reviewed statewide hospital discharge data for 1989-1995 (last year for which data are available) and identified a total of eight hospitalizations and no deaths during these years for hemosiderosis in infants less than one year of age. There were no more than 3 cases in any year and no geographic clustering.

On April 6, 1998, the American Academy of Pediatrics (AAP) Committee on Environmental Health released a statement concerning toxic effects of indoor molds and acute idiopathic pulmonary hemorrhage in infants. They recommend that until more information is available on the etiology of this condition, pediatricians should try to ensure that infants under 1 year of age are not exposed to chronically moldy, water-damaged environments.[16]

Sources of Additional Information/Assistance:

Environmental Health Investigations Branch, California Department of Health Services:
Sandra McNeel, D.V.M.; Debra Gilliss, M.D., M.P.H.; Richard Kreutzer, M.D.
(510) 450-3818

Fact Sheet "Mold in My Home: What Do I Do?" Indoor Air Quality Section California Department of Health Services, 2151 Berkeley Way (EHLB) Berkeley, CA 94704 *www.dhs.ca.gov/org/ps/deodc/ehlb/iaqs/*
510-540-2476 (copy enclosed).

Informative website on Stachybotrys maintained by Case Western Reserve University, where Cleveland children with pulmonary hemorrhage were cared for: *http://gcrc.cwru.edu/stachy*.

References

1. Kozak PP, Garvins J, Cummins LH, Gillman SA. Annals of Allergy 1980; 45:167-176.
2. Ueno Y, editor. General toxicology. In: Trichothecenes - chemical, biological and toxicological aspects. New York, NY: Elsevier Science Publishing Co., Inc., 1983:135-46.
3. Corrier DE. Mycotoxicosis: mechanism of immunosuppression. Vet Immunol Immunopathol 1991;30:73-87.
4. Jarvis BB, Salemme J, Morais A. Stachybotrys toxins. Natural Toxins 1995;3:10-16.
5. Jarvis BB, Yang C. Personal Communication. Discussion session. Fungi and Bacteria in Indoor Air Environments. Saratoga Springs, NY. October 6-7, 1994.
6. Flannigan B, McCabe EM, McGarry F. Allergenic and toxigenic micro-organisms in houses. J Appl Bact Symp (Suppl) 1991;70:61S-73S.
7. Forgacs J. Stachybotrys toxicosis. In: Kadis S, Ciegler A, Aji SJ, eds. Microbial Toxins: Volume VI-Fungal Toxins, New York: Academic Press, 1972:95-130.
8. Hintikka EL. Human stachybotrytoxicosis. In: Wylie TD, Morehouse LG, eds. Mycotoxigenic Fungi, Mycotoxins, Mycotoxicoses. New York: Marcel Dekker, 1987:87-89.
9. Croft WA, Jarvis BB, Yatawara CS. Airborne outbreak of trichothecene toxicosis. Atmospheric Environment 1986;20(3):549-52.
10. Johanning E, Morey PR, Jarvis BB. Clinical epidemiological investigation of health effects caused by *Stachybotrys chartarum* building contamination. Proceedings of Indoor Air, 1993;1:225-30.
11. Johanning E, Biagini R, et. al. Health and immunology study following exposure to toxigenic fungi (*Stachybotrys chartarum*) in a water-damaged office environment Int Arch Occup Environ Health 1996;68:207-18.
12. Hodgson MJ, et. al. Building-associated pulmonary disease from exposure to *Stachybotrys chartarum* and *Aspergillus versicolor*. J Occ Env Med. 1998;40:241-9.
13. Montana E, Etzel RA, Allan T, Horgan TE, Dearborn DG. Environmental risk factors associated with pediatric idiopathic pulmonary hemorrhage and hemosiderosis in a Cleveland community. Pediatrics 1997;99:E5 (electronic edition)
14. CDC. Update: pulmonary hemorrhage/hemosiderosis among infants - Cleveland, Ohio. 1993-1996. MMWR 1997;46:33-5.
15. Nikulin M, Reijula K, Jarvis BB, Hintikka EL. Experimental lung mucotoxicosis in mice induced by *Stachybotrys atra*. Int J Exp Path. 1996;77:213-8.
16. Nikulin M, Reijula K, Jarvis BB, Veijalainen P, Hintikka EL. Effects of intranasal exposure to spores of *Stachybotrys atra* in mice. Fund Appl Toxicol. 1997;35:182-8.
17. American Academy of Pediatrics. Toxic Effects of Indoor Molds. Pediatrics. 1998;101:712-4.

Reported by: Sandra McNeel, D.V.M., Environmental Health Investigations Branch, California Department of Health Services.

Note to Authors: Articles should be submitted to CM Editor, DCDC, CA Department of Health Services, 2151 Berkeley Way, Berkeley, CA 94704. Length should be approximately 1000 words or less. Tables, figures, and other materials can be included as supplements. References should be numbered sequentially. Submit typed, double-spaced hard copy of text and tables along with electronic copies, preferably in Word or Wordperfect, Macintosh or Windows, on a floppy disk. Graphics may be in a graphic format. Submissions can be e-mailed to *jrosenberg@dcdc2.dhs.cahwnet.gov*. Acknowledgments as to source will be provided, and may be individuals and/or programs as suggested. Publication in *CM* should not preclude publication elsewhere.